

**FIG. 1**

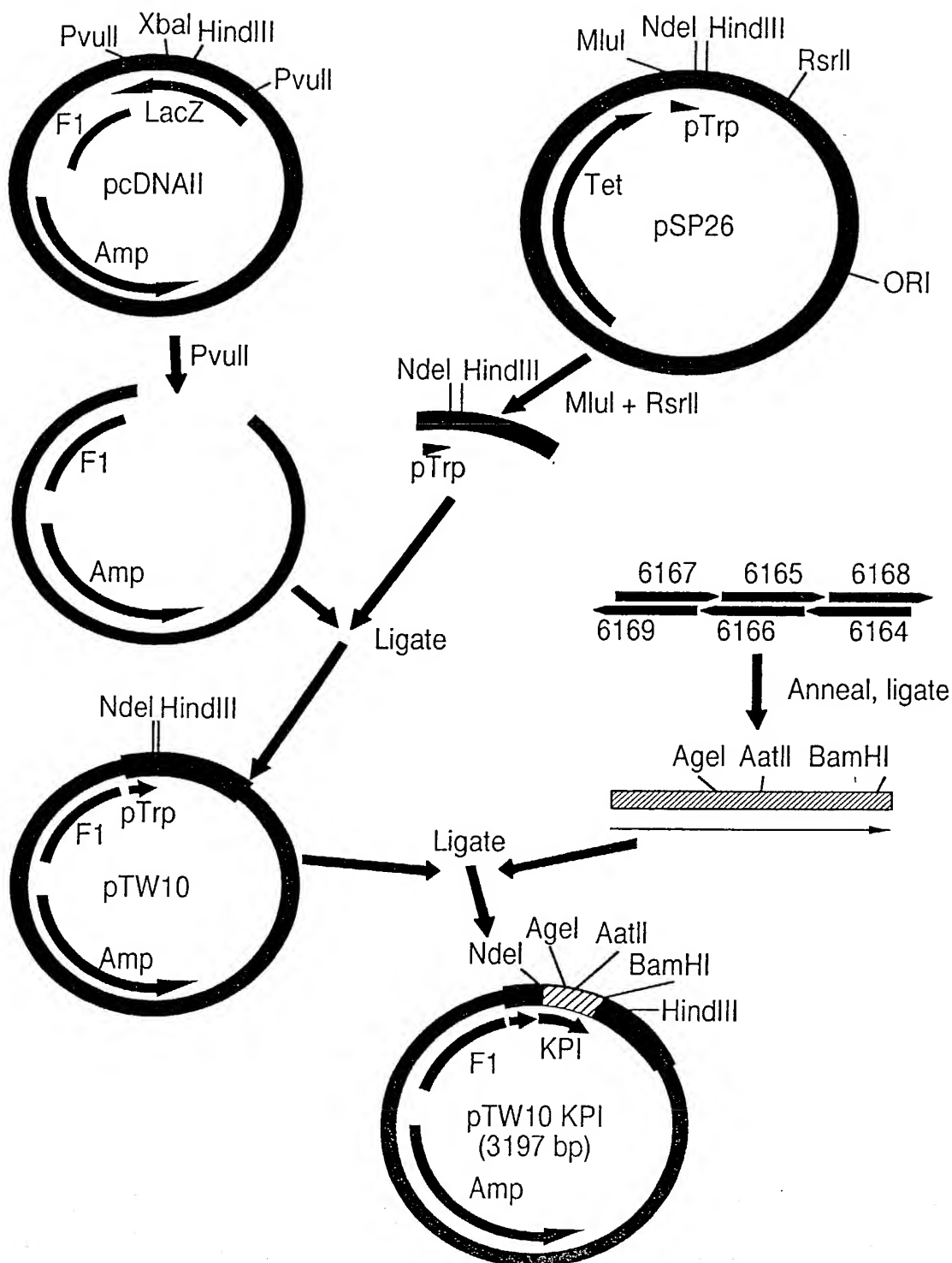
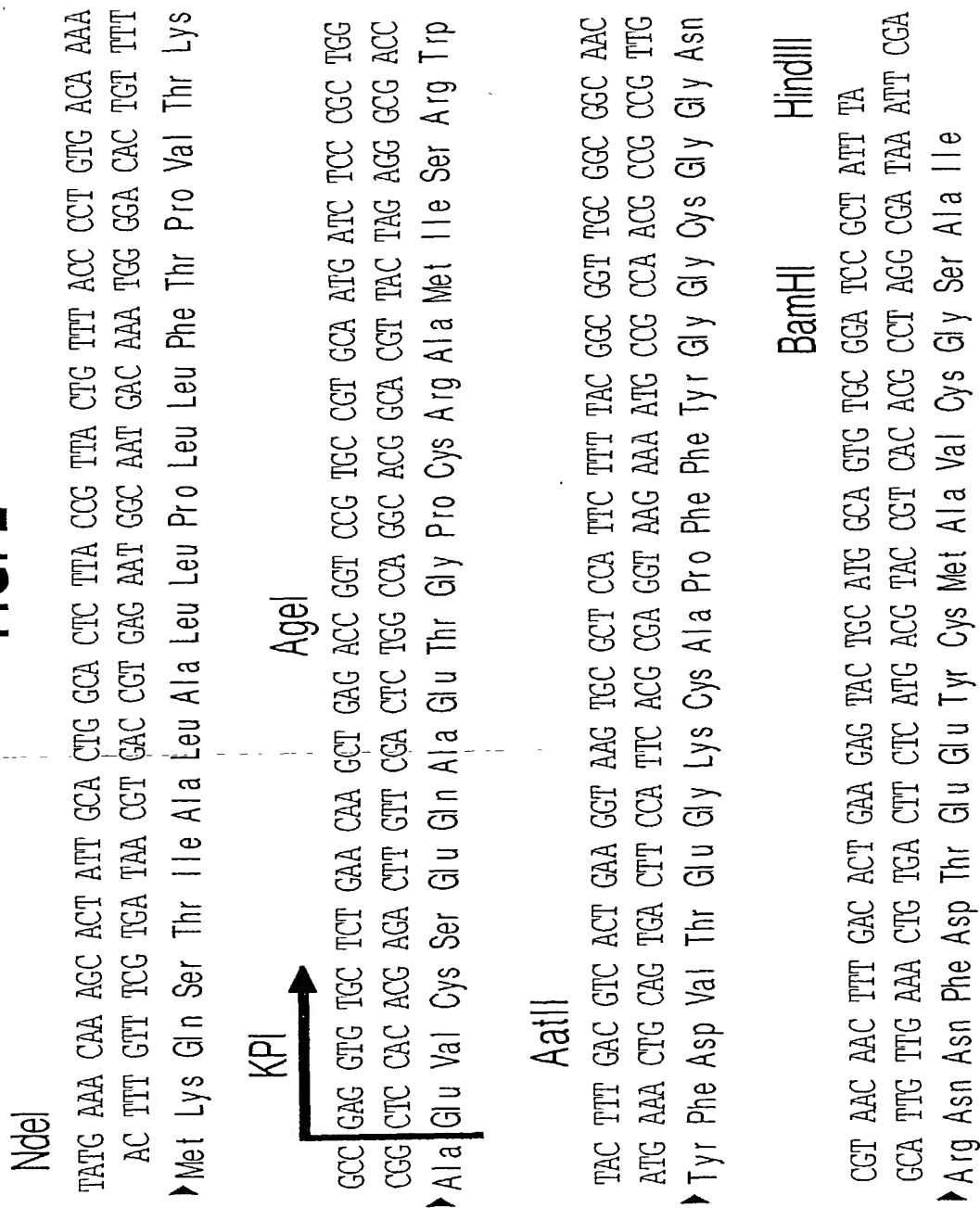


FIG. 2



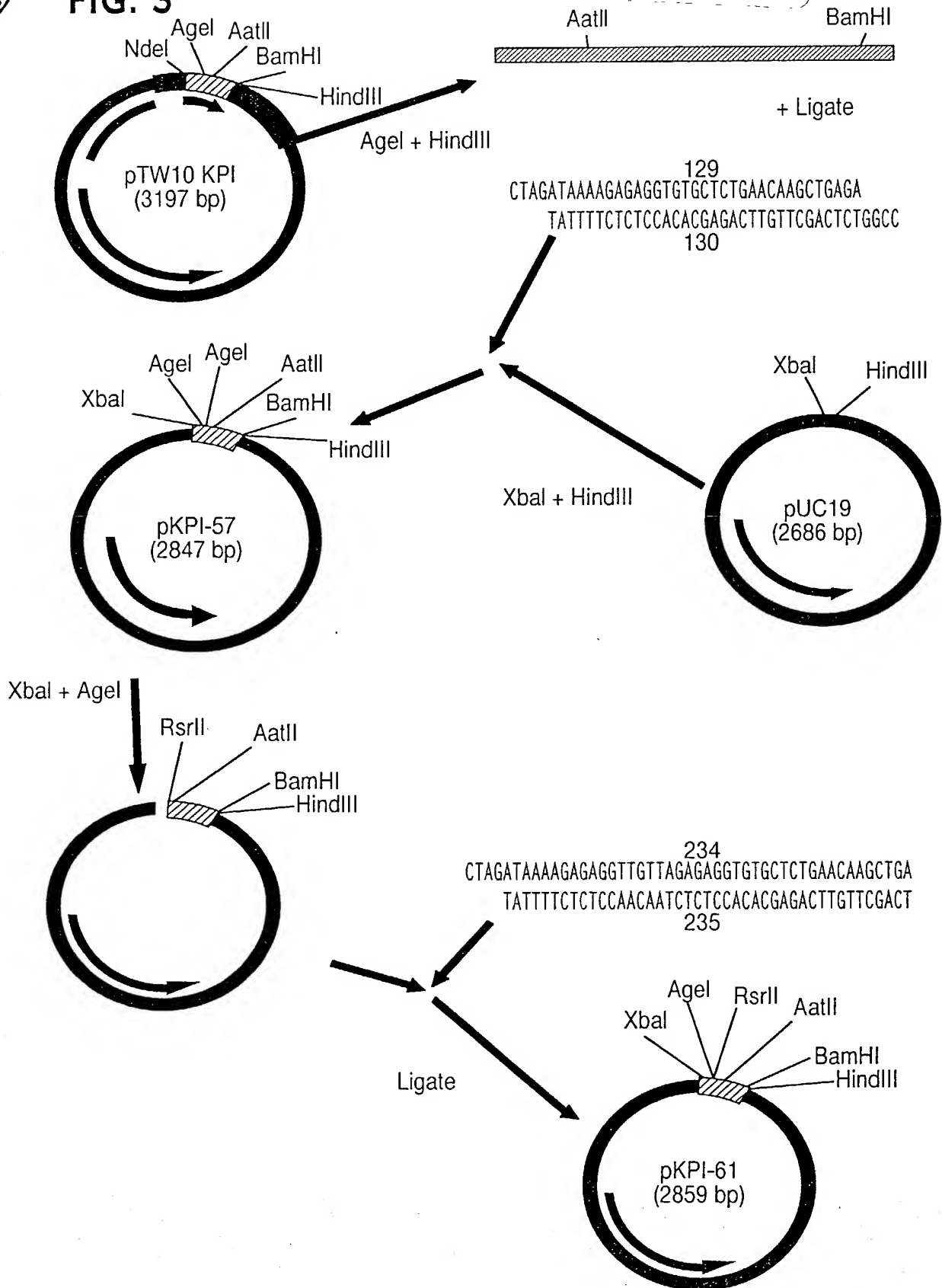
Title: PROTEASE INHIBITOR PEPTIDES  
 Inventor(s): R. Tyler WHITE et. al  
 Serial No. 10/076,604  
 DOCKET NO.: 056324-0129





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FIG. 3





# Aatli

TTC TTT TAC GGC GGT TGC GGC AAC CGT AAC TTT GAC ACT GAA GAG  
 AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT CTC  
 Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu

BamHI                      HindIII  
 TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA  
 ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA  
 Tyr Cys Met Ala Val Cys Gly Ser Ala Ile

$$\begin{aligned} & \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} \\ & \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} \end{aligned}$$



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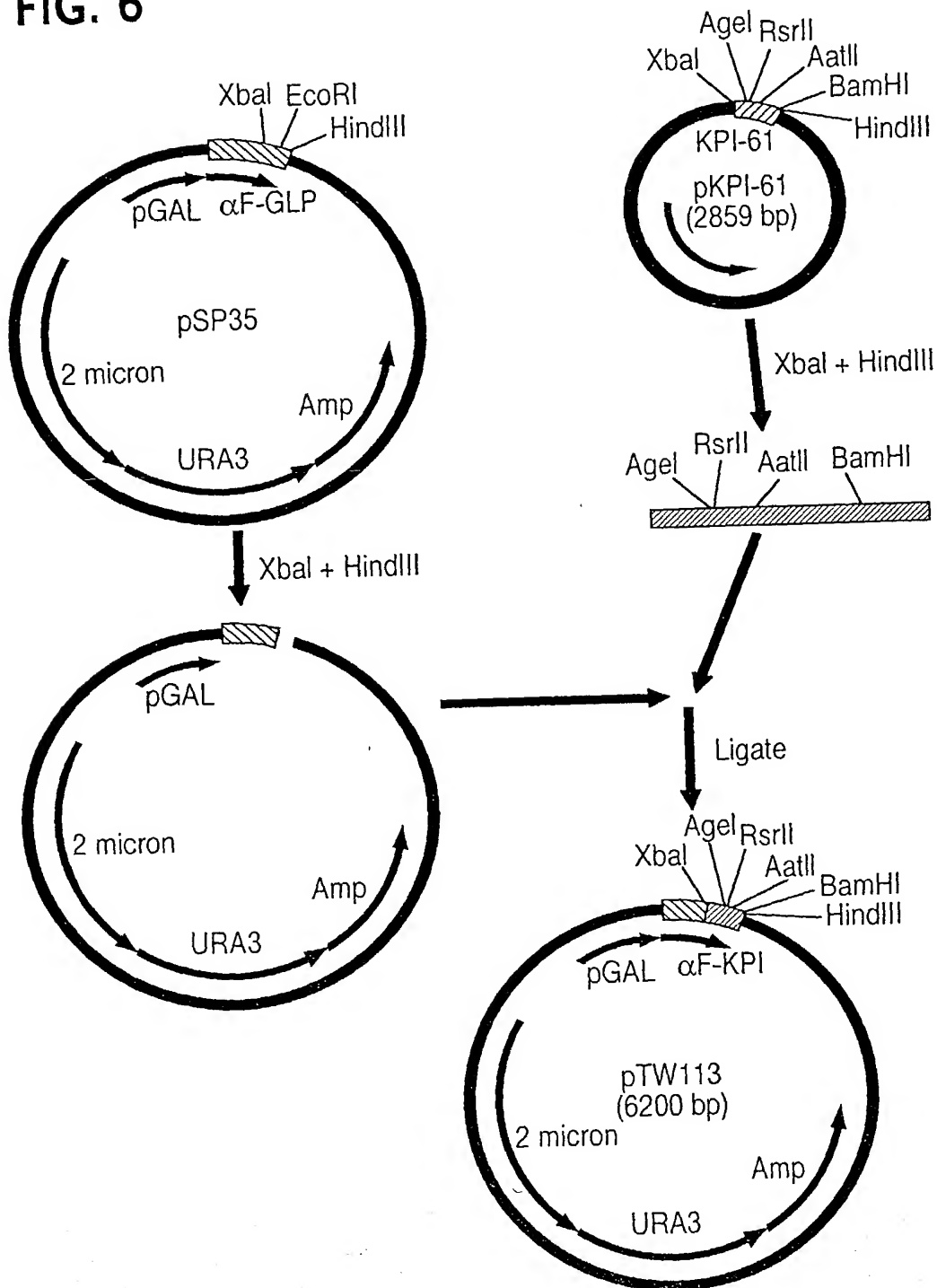
FIG. 5

KPI (-4-57)		RsrII	
XbaI	AgeI		
CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT			
TA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT CGA CTC TGG CCA			
▶ Leu Asp Lys Arg Glu Val Arg Glu Val Oys Ser Glu Glu Ala Glu Thr Gly			
		AatII	
CCG TGC CGT GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA GGT AAG TGC			
GGC ACG GCA CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT CCA TTC ACG			
▶ Pro Oys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Oys			
		BamHI	
GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC ACT GAA			
CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG TGA CTT			
▶ Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu			
		HindIII	
GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TA			
CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA			
▶ Glu Tyr Oys Met Ala Val Oys Gly Ser Ala Ile			



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FIG. 6





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## FIG. 7

 $\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC TAG AGG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



3,611,604 B2

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## FIG. 8

KPI(-4-57)

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - Ile - Ser - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57





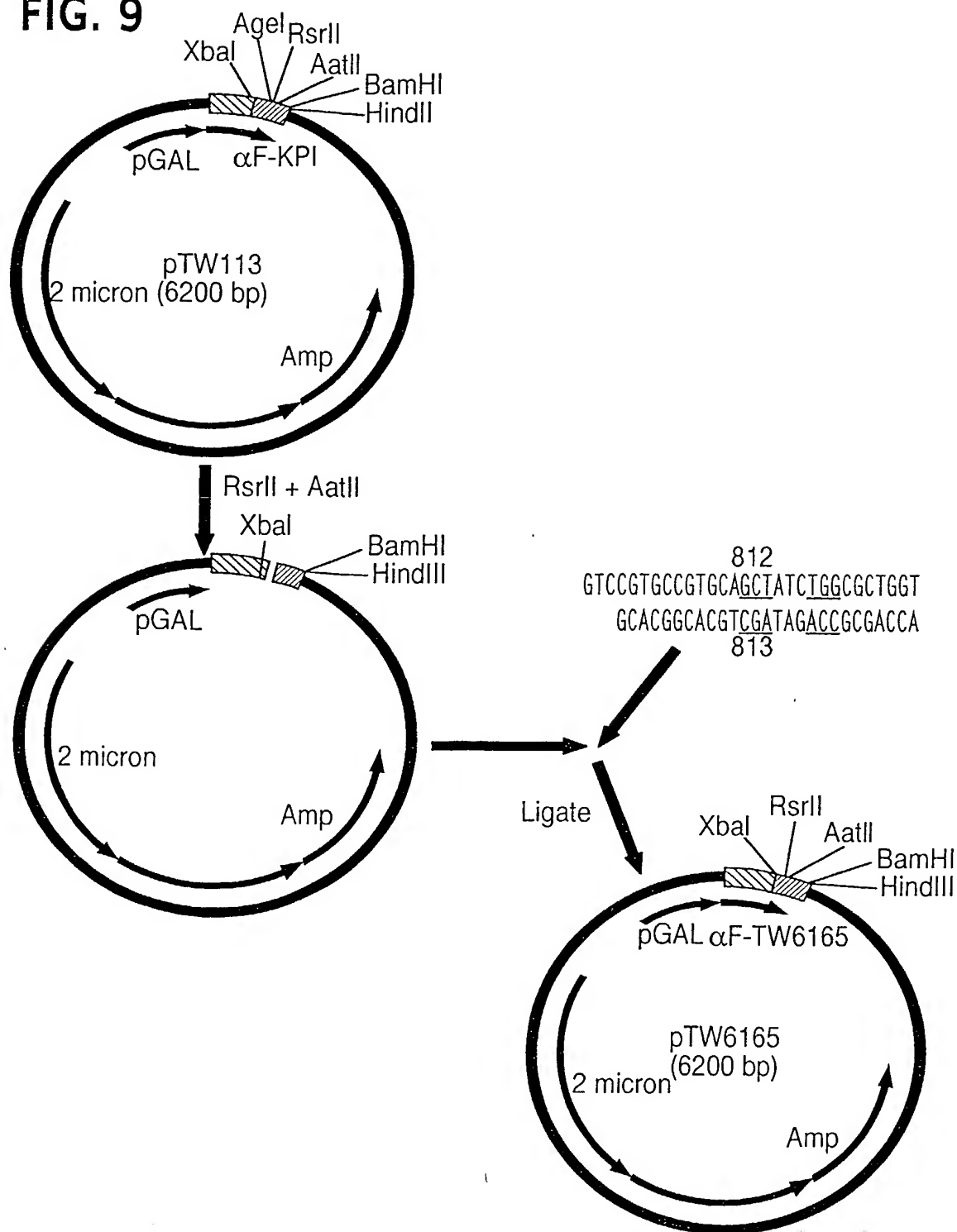
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**FIG. 9**





Title: PROTEASE INHIBITOR PEPTIDES

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pTW 6165

## FIG. 10

$\alpha$ -factor

→

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TGG CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ACC GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Trp Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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## FIG. 11

812

GTCCGTGCGGTGCAGCTATCTGGCGCTGGTACTTTGAAGT pTW6165 KPI(-4-57; M15A, S17F)  
GCAAGGCAAGTGCATAGACCGGCAACATGAAAC

813

814

GTCCGTGCGGTGCAGCTATCTACCGCTGGTACTTTGAAGT pTW6166 KPI(-4-57; M15A, S17Y)  
GCAAGGCAAGTGCATAGATGGGCAACATGAAAC

815

867

GTCCGTGCGGTGCATTGATCTTCGGCTGGTACTTTGAAGT pTW6175 KPI(-4-57; M15L, S17F)  
GCAAGGCAAGTAAGTAGAGGCAACATGAAAC

868

1493

GTCCGTGCGGTGCATTGATCTACCGCTGGTACTTTGAAGT pBG028 KPI(-4-57; M15L, S17Y)  
GCAAGGCAAGTAAGTAGATGGGCAACATGAAAC

1494

925

GTCCGTGCGGTGCAATGCACTTCGGCTGGTACTTTGAAGT pTW6183 KPI(-4-57; I16H, S17F)  
GCAAGGCAAGTTAAGTGAAGGCAACATGAAAC

926

927

GTCCGTGCGGTGCAATGCACTACCGCTGGTACTTTGAAGT pTW6184 KPI(-4-57; I16H, S17Y)  
GCAAGGCAAGTTAAGTGATGGGCAACATGAAAC

928

929

GTCCGTGCGGTGCAATGCACTGGCGCTGGTACTTTGAAGT pTW6185 KPI(-4-57; I16H, S17W)  
GCAAGGCAAGTTAAGTGACCGGCAACATGAAAC

930

863

GTCCGTGCGGTGCAGCTCACTCCCGCTGGTACTTTGAAGT pTW6173 KPI(-4-57; M15A, I16H)  
GCAAGGCAAGTGCAGTGAGGGCAACATGAAAC

864

865

GTCCGTGCGGTGCATTGCACTCCCGCTGGTACTTTGAAGT pTW6174 KPI(-4-57; M15L, I16H)  
GCAAGGCAAGTAAGTGAGGGCAACATGAAAC

866



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# FIG. 12

pTW 6166

$\alpha$ -factor

→  
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, S17Y)

→  
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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pTW 6175

## FIG. 13

$\alpha$ -factor

→  
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, S17F)

→  
GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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## FIG. 14

pBG028

$\alpha$ -factor

→

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG ATC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC TAG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu Ile Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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# FIG. 15

pTW6183

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; I16H, S17F)

XbaI

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Phe Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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pTW6184

## FIG. 16

 $\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17Y)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TAC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ATG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Tyr Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile





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pTW6185

## FIG. 17

$\alpha$ -factor

→  
ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; I16H, S17W)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA ATG CAC TGG CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT TAC GTG ACC GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Met His Trp Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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pTW6173

# FIG. 18

$\alpha$ -factor



ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala  
  
GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val  
  
ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn  
  
AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15A, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala His Ser Arg Trp Tyr Phe Asp Val Thr Glu  
  
GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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Inventor(s): R. Tyler WHITE et. al

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pTW6174

## FIG. 19

 $\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

XbaI

KPI(-4-57; M15L, I16H)

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA TTG CAC TCC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT AAC GTG AGG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Leu His Ser Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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## FIG. 20

KPI(-4-57; M15A, S17W) TW6165

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Trp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



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## FIG. 21

KPI(-4-57; M15A, S17Y) TW6166

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Tyr - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



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Inventor(s): R. Tyler WHITE et. al  
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## FIG. 22

KPI(-4-57; M15L, S17F) TW6175

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



056324-0129

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Inventor(s): R. Tyler WHITE et. al  
Serial No. 10/076,604  
DOCKET NO.: 056324-0129

## FIG. 23

KPI(-4-57; M15L, S17Y) BG028

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - Ile - Tyr - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



Title: PROTEASE INHIBITOR PEPTIDES

Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

DOCKET NO.: 056324-0129

## FIG. 24

KPI(-4-57; I16H, S17F) TW6183

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

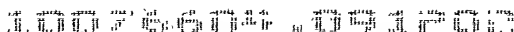
Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57





Inventor(s): R. Tyler WHITE et. al  
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Val - Cys - Gly - Ser - Ala - Ile  
52      53      54      55      56      57



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Serial No. 10/076,604  
DOCKET NO.: 056324-0129

## FIG. 26

KPI(-4-57; I16H, S17W) TW6185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Met - His - Trp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



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Inventor(s): R. Tyler WHITE et. al  
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DOCKET NO.: 056324-0129

## FIG. 27

KPI(-4-57; M15A, S17F) DD185

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - Ile - Phe - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



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Inventor(s): R. Tyler WHITE et. al  
Serial No. 10/076,604  
DOCKET NO.: 056324-0129

## FIG. 28

KPI(-4-57; M15A, I16H) TW6173

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Ala - His - SerTrp - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57

Title: PROTEASE INHIBITOR PEPTIDES

Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

DOCKET NO.: 056324-0129

## FIG. 29

KPI(-4-57; M15L, I16H) TW6174

Glu - Val - Val - Arg - Glu - Val - Cys - Ser - Glu - Gln - Ala  
-4 -3 -2 -1 1 2 3 4 5 6 7

Glu - Thr - Gly - Pro - Cys - Arg - Ala - Leu - His - Ser - Arg  
8 9 10 11 12 13 14 15 16 17 18

Trp - Tyr - Phe - Asp - Val - Thr - Glu - Gly - Lys - Cys - Ala  
19 20 21 22 23 24 25 26 27 28 29

Pro - Phe - Phe - Tyr - Gly - Gly - Cys - Gly - Gly - Asn - Arg  
30 31 32 33 34 35 36 37 38 39 40

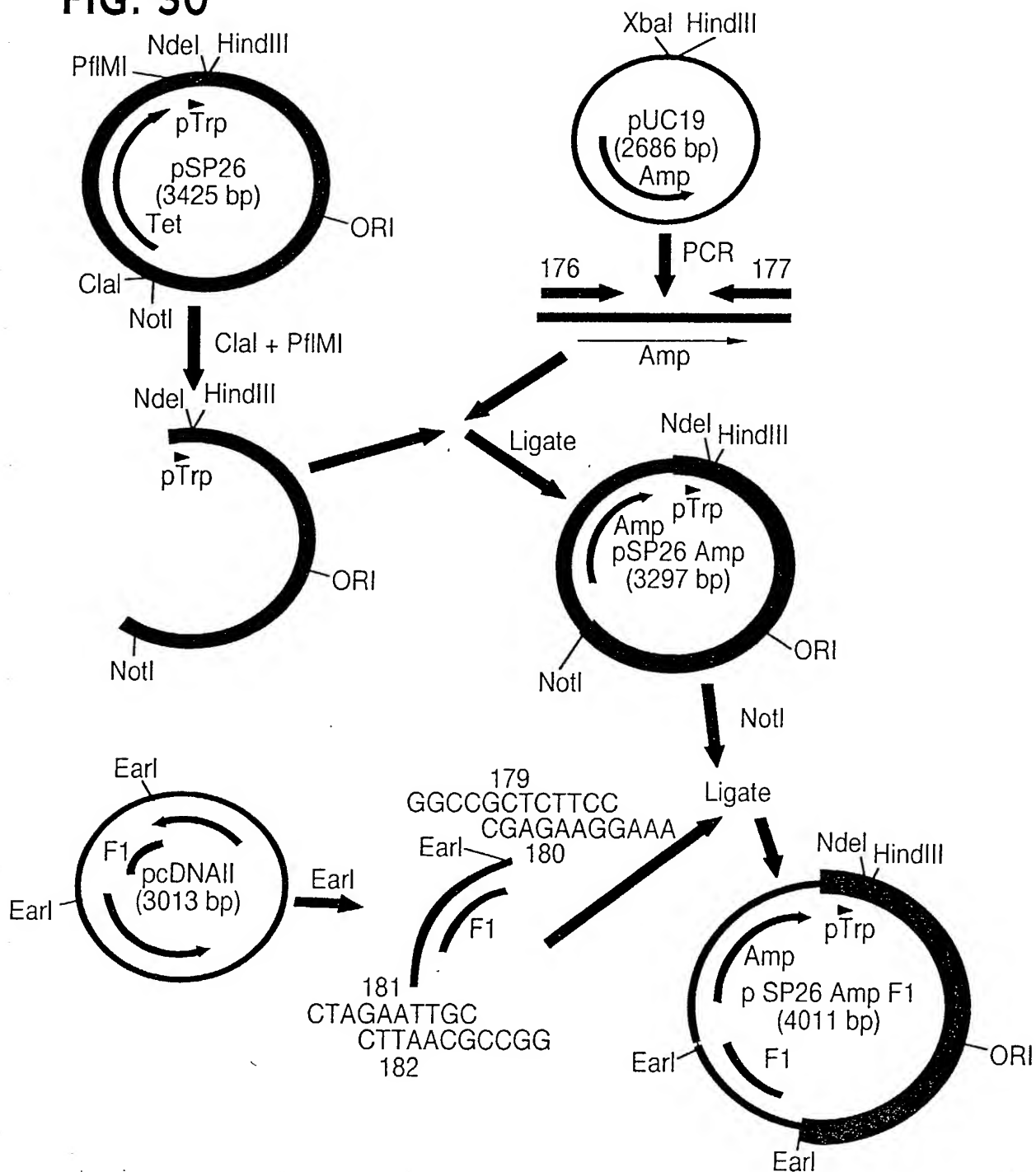
Asn - Asn - Phe - Asp - Thr - Glu - Glu - Tyr - Cys - Met - Ala  
41 42 43 44 45 46 47 48 49 50 51

Val - Cys - Gly - Ser - Ala - Ile  
52 53 54 55 56 57



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DOCKET NO.: 056324-0129

FIG. 30



O I P E  
SEP 12 2002  
PATENT & TRADEMARK OFFICE

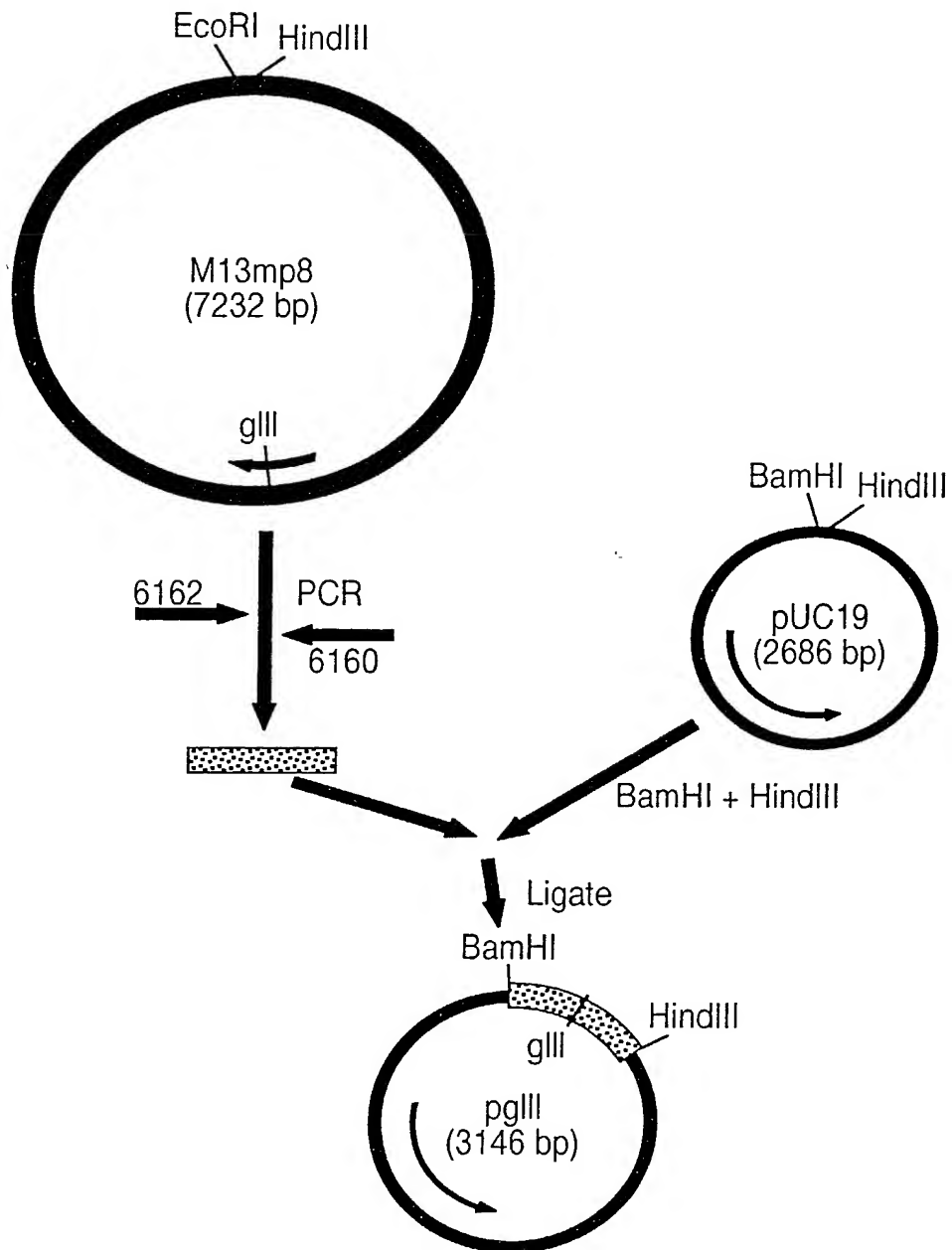
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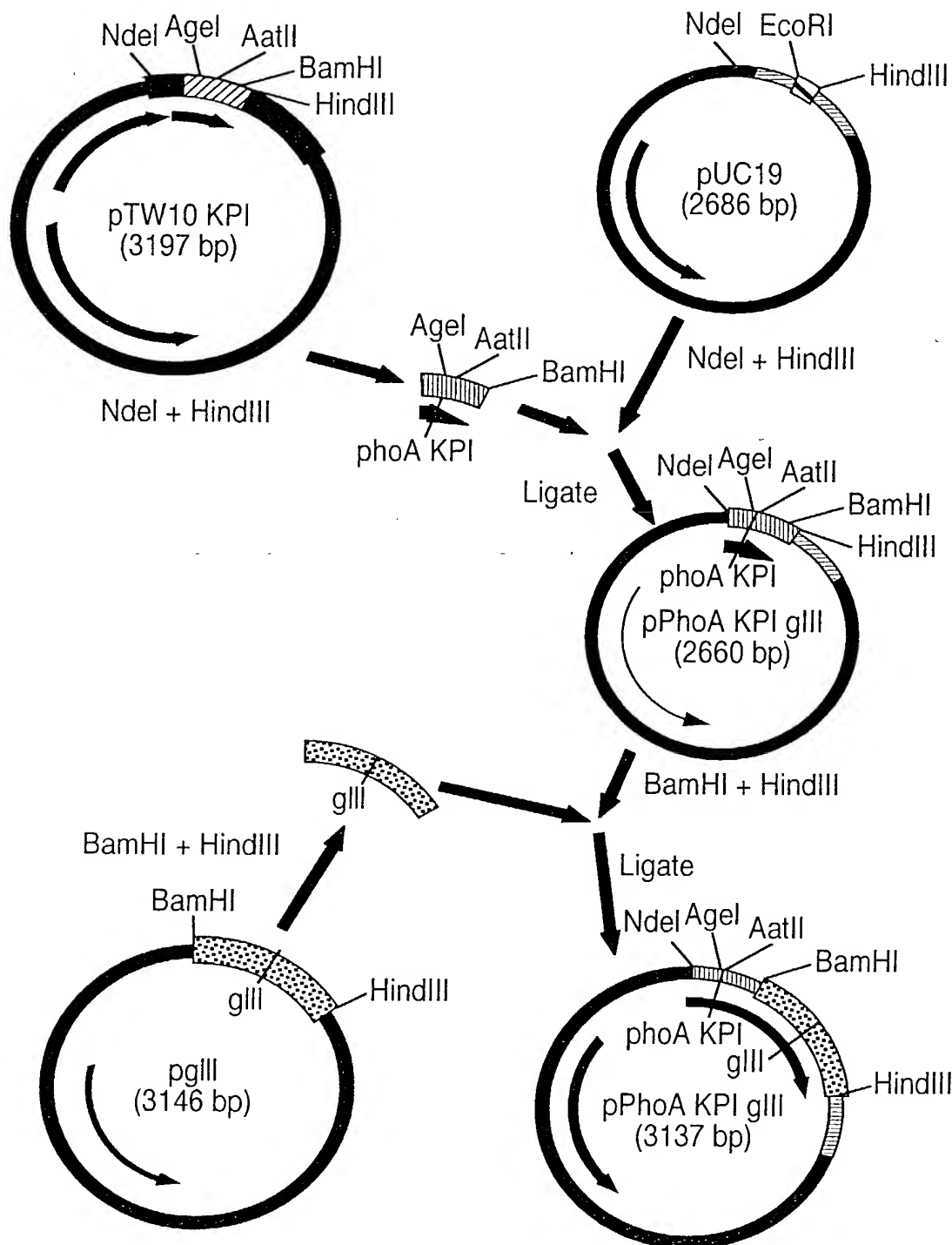
FIG. 31





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FIG. 32

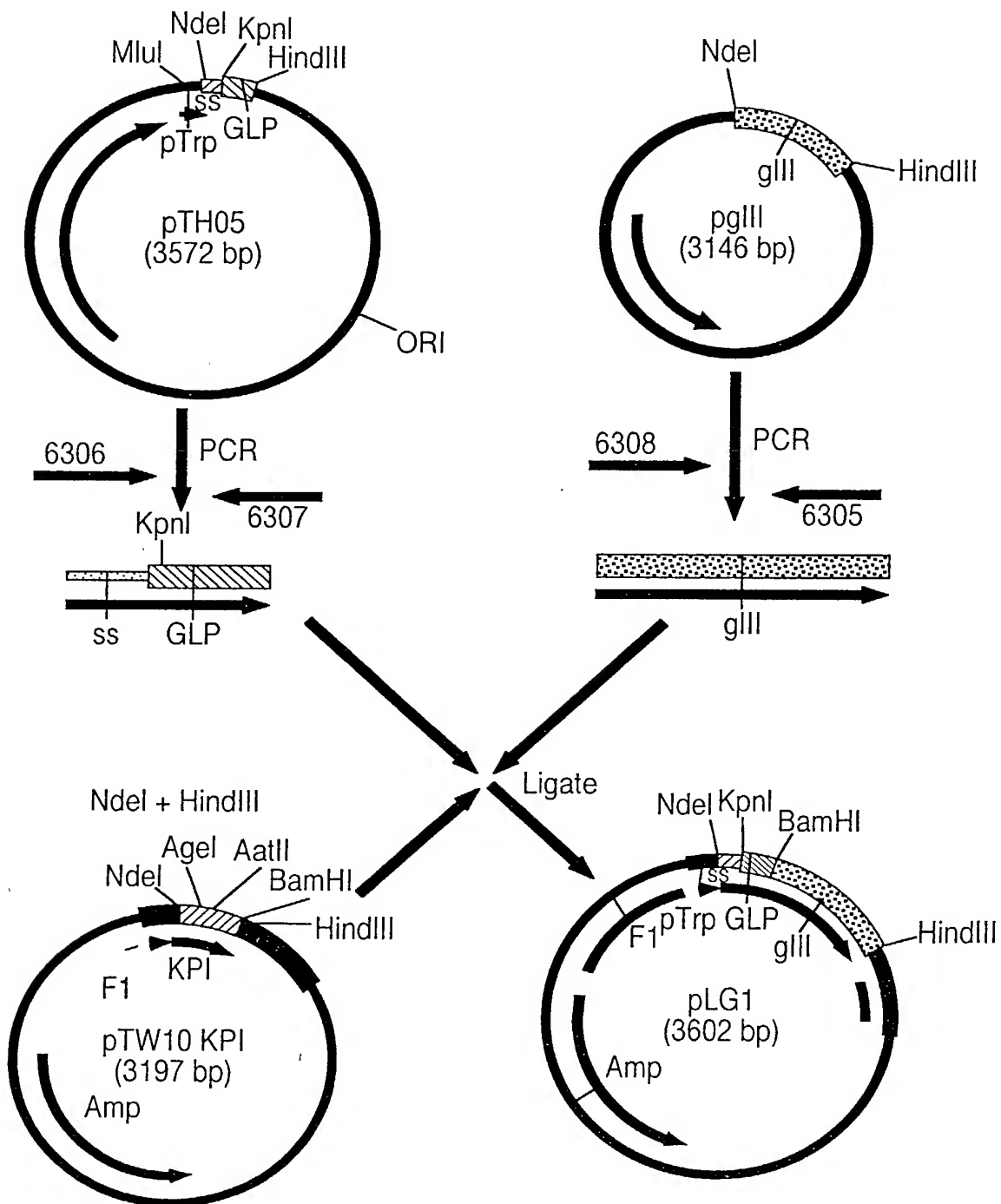






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FIG. 33





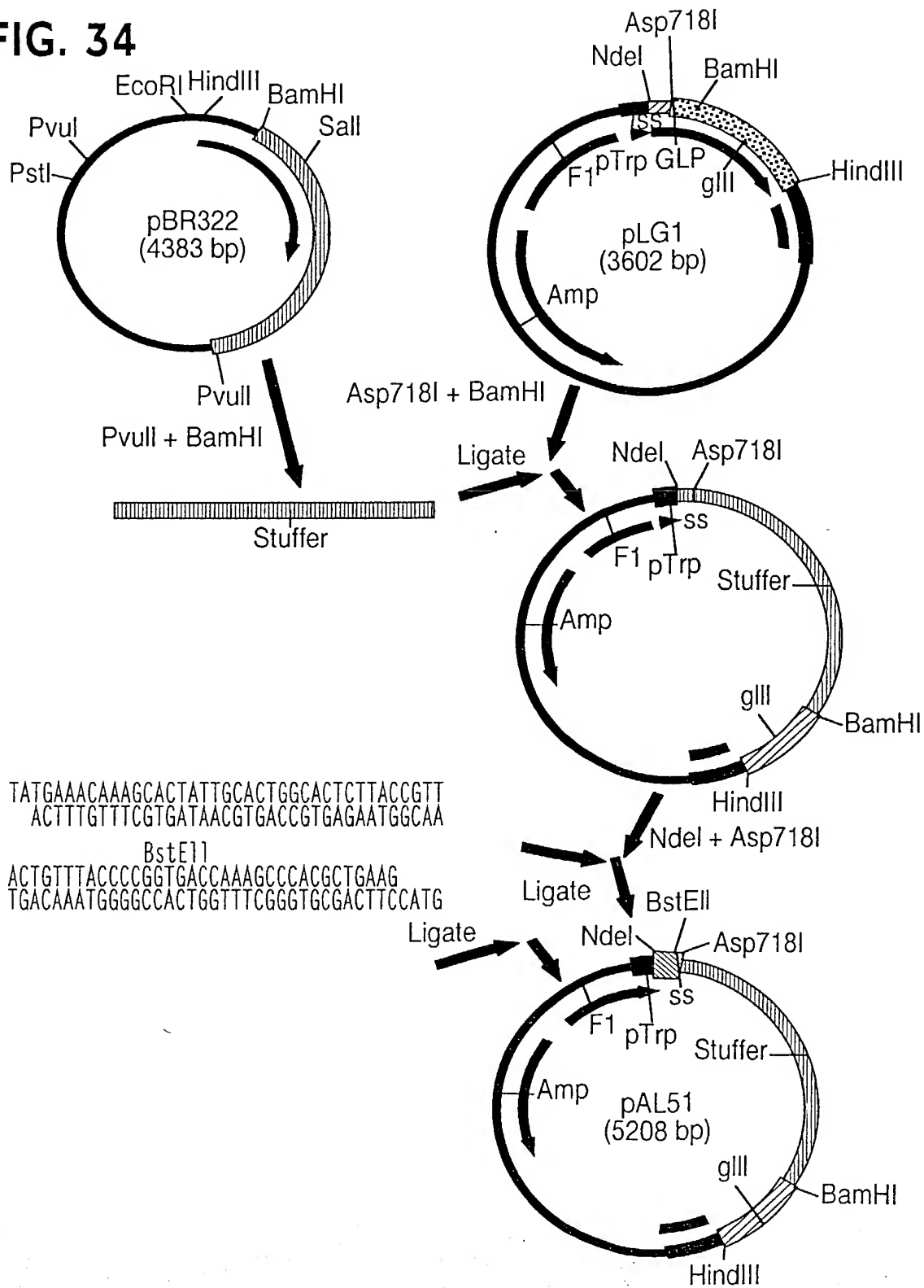
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**FIG. 34**



6512

6513

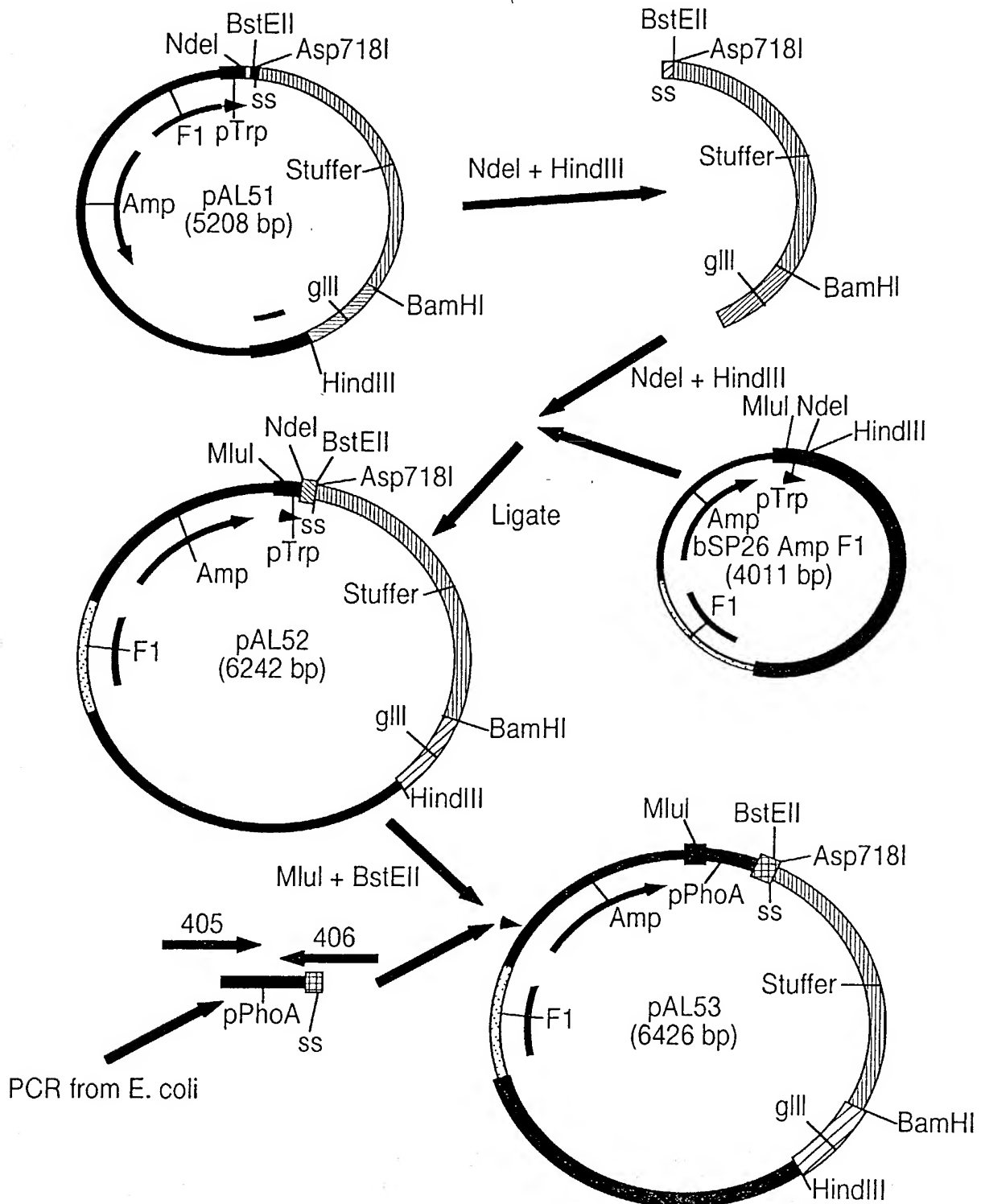
TATGAAACAAAGCACTATTGCACTGGCACTCTTACCGTT  
ACTTTGTTTCGTGATAACGTGACCGTGAGAATGGCAA

BstEII  
ACTGTTTACCCGGTGACCAAGCCACGCTGAAG  
TGACAAATGGGGCCACTGGTTTCGGGTGCGACTTCCATG



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FIG. 35





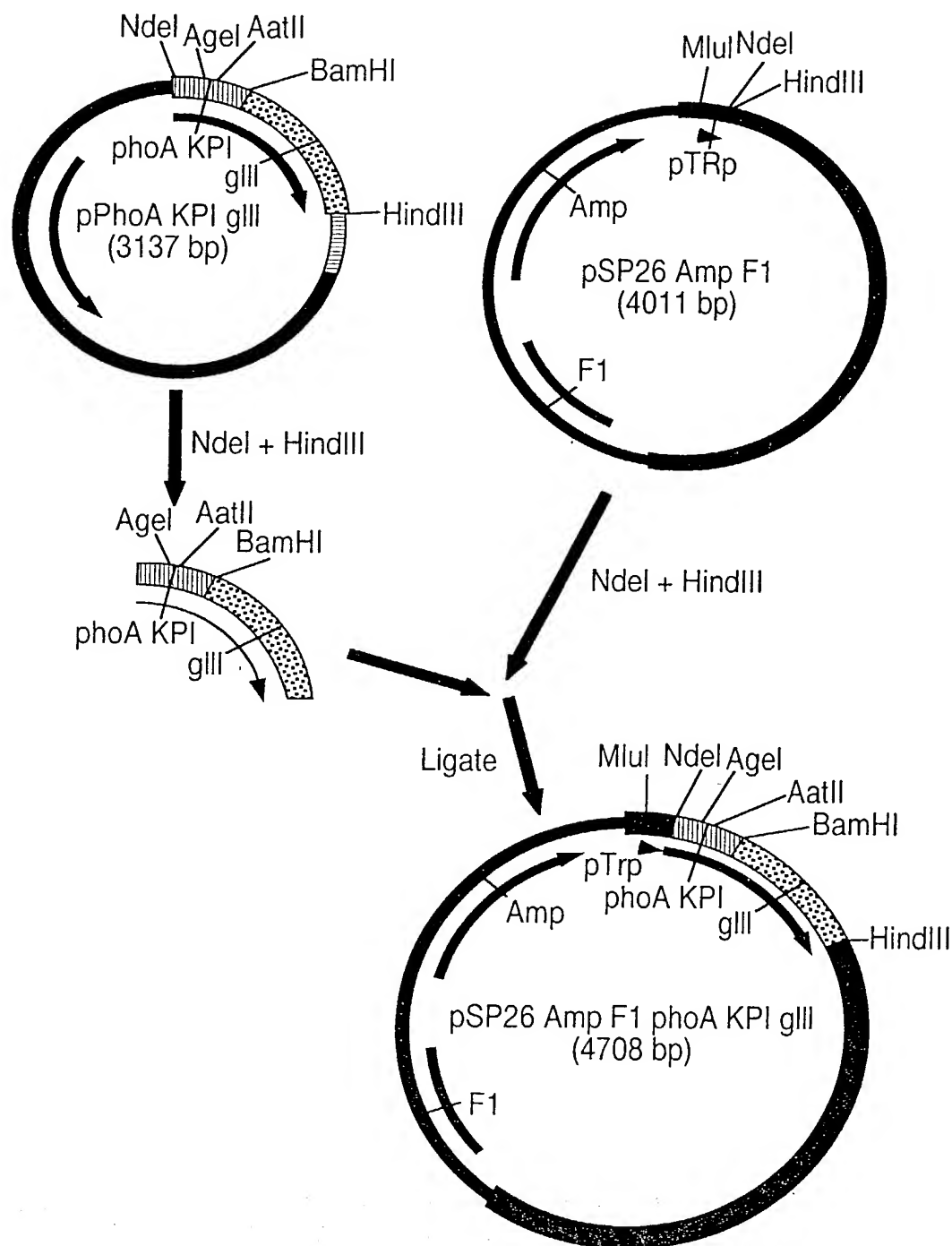
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Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

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FIG. 36





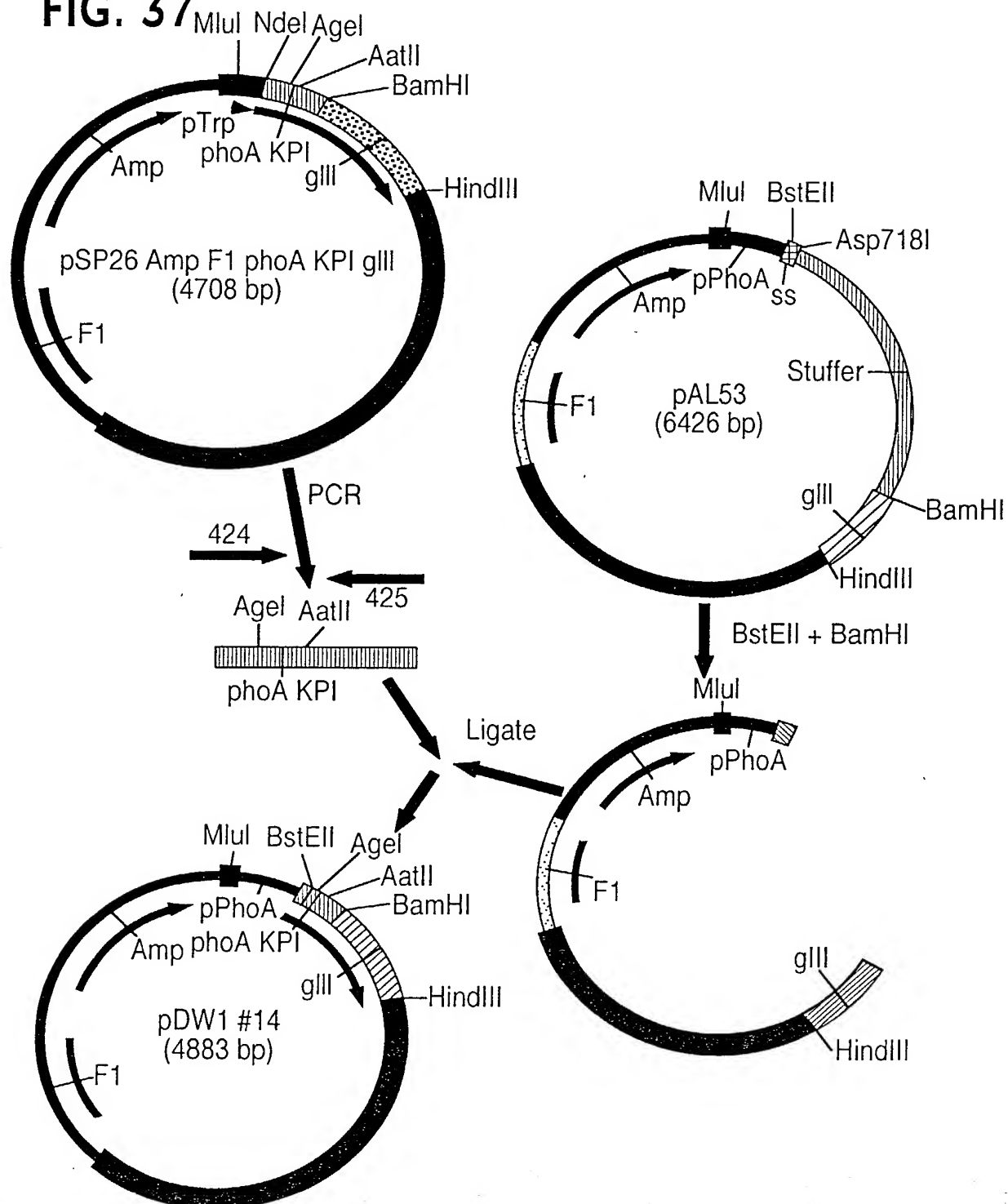
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FIG. 37





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FIG. 38

phoA signal →

BstEII

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI (1-55) →

Agel

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA ATG ATC TCC CGC TGG  
▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile Ser Arg Trp

AatII

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC  
▶ Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn

BamHI gIII →

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT  
▶ Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA  
▶ Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT  
▶ Asn Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT  
▶ Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT  
▶ Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA  
▶ Asn Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu

TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA  
▶ Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

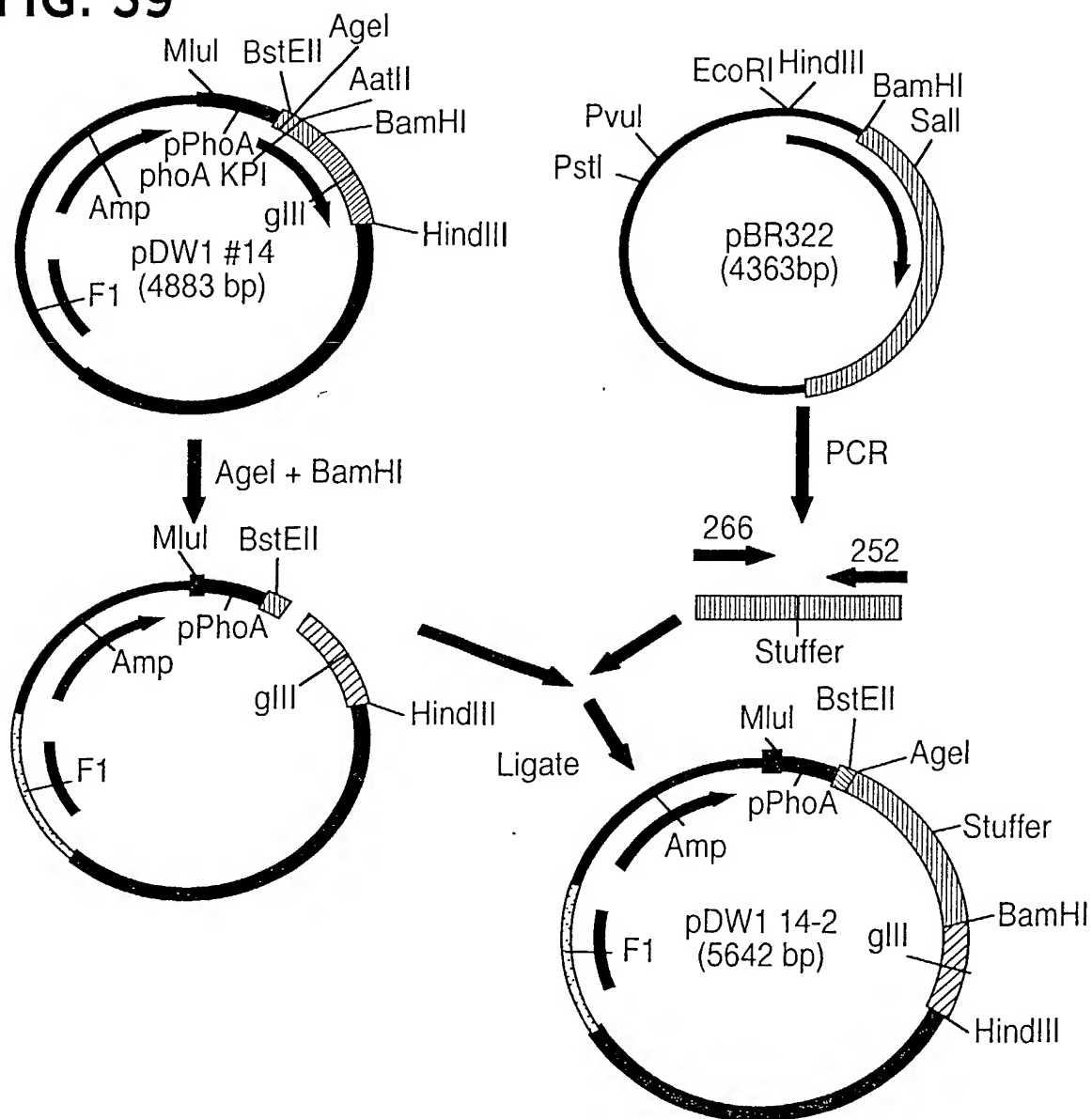
ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA  
▶ Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
▶ Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser • •



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Inventor(s): R. Tyler WHITE et. al  
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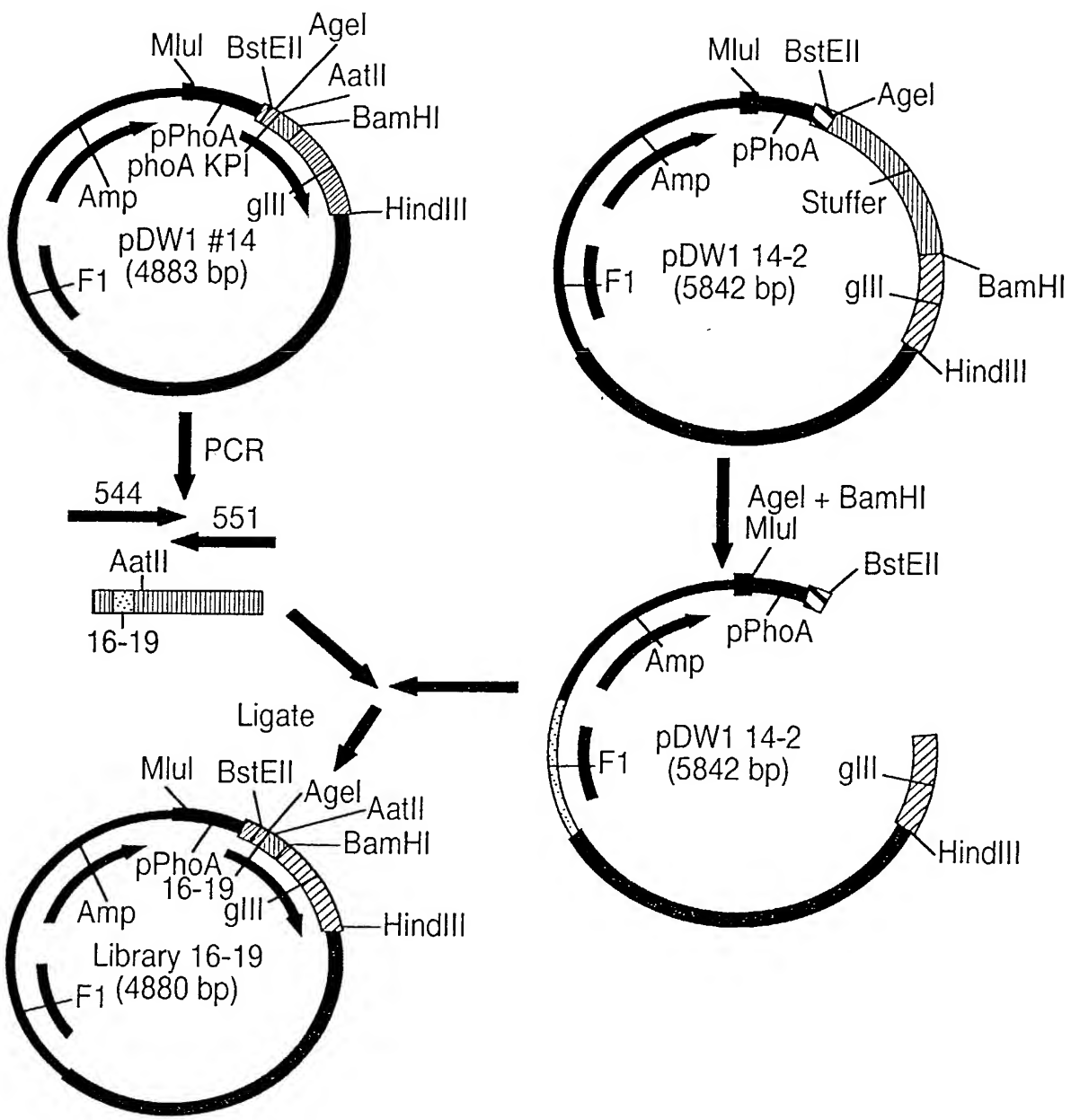
FIG. 39



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Serial No. 10/076,604  
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FIG. 40







Title: PROTEASE INHIBITOR PEPTIDES

Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

DOCKET NO.: 056324-0129

phoA signal

## FIG. 41

BstEII

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI (1-55; 16 - 19)

AgeI

16 - 19

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT NNS NNS NNS NNS TGG TAC  
▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg --- --- --- --- Trp Tyr

AatII

TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT  
▶ Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg

BamHI

gIII

AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT GGT  
▶ Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser Gly

TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA AAT  
▶ Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu Asn

GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT GAT  
▶ Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr Asp

TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT GGT  
▶ Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn Gly

gIII

GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT AAT  
▶ Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp Asn

TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA TGT  
▶ Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu Cys

CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA ATA  
▶ Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys Ile

AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA TTT  
▶ Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val Phe

TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
▶ Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser ...



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phoA signal

## FIG. 42

BstEII

GTG AAA CAA AGC ACT ATT GCA CTG GCA CTC TTA CCG TTA CTG TTT ACC CCG GTG ACC AAA  
▶ Val Lys Gln Ser Thr Ile Ala Leu Ala Leu Leu Pro Leu Leu Phe Thr Pro Val Thr Lys

KPI (1-55; M15A, S17F)

Agel

GCC GAG GTG TGC TCT GAA CAA GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG  
▶ Ala Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp

AatII

TAC TTT GAC GTC ACT GAA GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC  
▶ Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn

BamHI

gIII

CGT AAC AAC TTT GAC ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GGT GGT GGC TCT  
▶ Arg Asn Asn Phe Asp Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Gly Gly Gly Ser

GGT TCC GGT GAT TTT GAT TAT GAA AAG ATG GCA AAC GCT AAT AAG GGG GCT ATG ACC GAA  
▶ Gly Ser Gly Asp Phe Asp Tyr Glu Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu

AAT GCC GAT GAA AAC GCG CTA CAG TCT GAC GCT AAA GGC AAA CTT GAT TCT GTC GCT ACT  
▶ Asn Ala Asp Glu Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr

GAT TAC GGT GCT GCT ATC GAT GGT TTC ATT GGT GAC GTT TCC GGC CTT GCT AAT GGT AAT  
▶ Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu Ala Asn Gly Asn

GGT GCT ACT GGT GAT TTT GCT GGC TCT AAT TCC CAA ATG GCT CAA GTC GGT GAC GGT GAT  
▶ Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln Met Ala Gln Val Gly Asp Gly Asp

AAT TCA CCT TTA ATG AAT AAT TTC CGT CAA TAT TTA CCT TCC CTC CCT CAA TCG GTT GAA  
▶ Asn Ser Pro Leu Met Asn Asn Phe Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu

TGT CGC CCT TTT GTC TTT GGC GCT GGT AAA CCA TAC GAA TTT TCT ATT GAT TGT GAC AAA  
▶ Cys Arg Pro Phe Val Phe Gly Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys

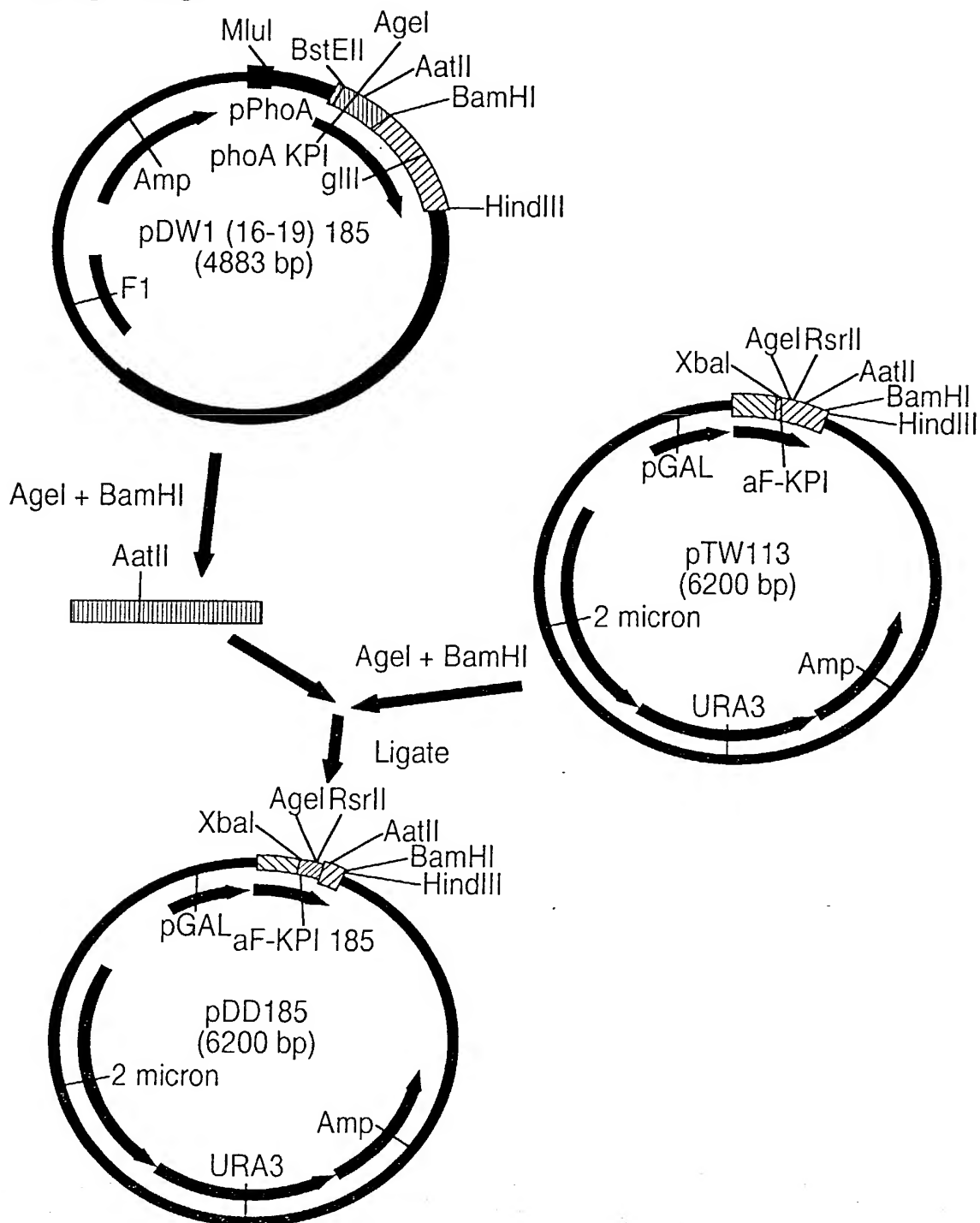
ATA AAC TTA TTC CGT GGT GTC TTT GCG TTT CTT TTA TAT GTT GCC ACC TTT ATG TAT GTA  
▶ Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr Phe Met Tyr Val

TTT TCT ACG TTT GCT AAC ATA CTG CGT AAT AAG GAG TCT TAA TA  
▶ Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu Ser



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FIG. 43





Title: PROTEASE INHIBITOR PEPTIDES

Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

DOCKET NO.: 056324-0129

pDD185

# FIG. 44

$\alpha$ -factor

ATG AGA TTT CCT TCA ATT TTT ACT GCA GTT TTA TTC GCA GCA TCC TCC GCA TTA GCT  
TAC TCT AAA GGA AGT TAA AAA TGA CGT CAA AAT AAG CGT CGT AGG AGG CGT AAT CGA  
▶ Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala

GCT CCA GTC AAC ACT ACA ACA GAA GAT GAA ACG GCA CAA ATT CCG GCT GAA GCT GTC  
CGA GGT CAG TTG TGA TGT TGT CTT CTA CTT TGC CGT GTT TAA GGC CGA CTT CGA CAG  
▶ Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala Glu Ala Val

ATC GGT TAC TTA GAT TTA GAA GGG GAT TTC GAT GTT GCT GTT TTG CCA TTT TCC AAC  
TAG CCA ATG AAT CTA AAT CTT CCC CTA AAG CTA CAA CGA CAA AAC GGT AAA AGG TTG  
▶ Ile Gly Tyr Leu Asp Leu Glu Gly Asp Phe Asp Val Ala Val Leu Pro Phe Ser Asn

AGC ACA AAT AAC GGG TTA TTG TTT ATA AAT ACT ACT ATT GCC AGC ATT GCT GCT AAA  
TCG TGT TTA TTG CCC AAT AAC AAA TAT TTA TGA TGA TAA CGG TCG TAA CGA CGA TTT  
▶ Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys

KPI(-4-57; M15A, S17F)

XbaI

GAA GAA GGG GTA TCT CTA GAT AAA AGA GAG GTT GTT AGA GAG GTG TGC TCT GAA CAA  
CTT CTT CCC CAT AGA GAT CTA TTT TCT CTC CAA CAA TCT CTC CAC ACG AGA CTT GTT  
▶ Glu Glu Gly Val Ser Leu Asp Lys Arg Glu Val Val Arg Glu Val Cys Ser Glu Gln

RsrII

AgeI

AatII

GCT GAG ACC GGT CCG TGC CGT GCA GCT ATC TTC CGC TGG TAC TTT GAC GTC ACT GAA  
CGA CTC TGG CCA GGC ACG GCA CGT CGA TAG AAG GCG ACC ATG AAA CTG CAG TGA CTT  
▶ Ala Glu Thr Gly Pro Cys Arg Ala Ala Ile Phe Arg Trp Tyr Phe Asp Val Thr Glu

GGT AAG TGC GCT CCA TTC TTT TAC GGC GGT TGC GGC GGC AAC CGT AAC AAC TTT GAC  
CCA TTC ACG CGA GGT AAG AAA ATG CCG CCA ACG CCG CCG TTG GCA TTG TTG AAA CTG  
▶ Gly Lys Cys Ala Pro Phe Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp

BamHI

HindIII

ACT GAA GAG TAC TGC ATG GCA GTG TGC GGA TCC GCT ATT TAA GCT T  
TGA CTT CTC ATG ACG TAC CGT CAC ACG CCT AGG CGA TAA ATT CGA A  
▶ Thr Glu Glu Tyr Cys Met Ala Val Cys Gly Ser Ala Ile



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## FIG. 45

Plasma kallikrein inhibition by KPI (-4-57) variants

<u>Variant</u>	<u>Substitution</u>			<u>K<sub>i</sub>(nM)</u>
	15	16	17	
TW113	KPI (-4-57)			45.00
DD185	KPI (-4-57; M15A, S17F)	A	F	0.39
TW6165	KPI (-4-57; M15A, S17W)	A	W	0.65
TW6166	KPI (-4-57; M15A, S17Y)	A	Y	0.40
TW6175	KPI (-4-57; M15L, S17F)	L	F	0.50
BG028	KPI (-4-57; M15L, S17Y)	L	Y	1.10
TW6183	KPI (-4-57; I16H, S17F)		F	1.20
TW6184	KPI (-4-57; I16H, S17Y)		Y	0.91
TW6185	KPI (-4-57; I16H, S17W)		W	1.30
TW6173	KPI (-4-57; M15A, I16H)	A		1.00
TW6174	KPI (-4-57; M15L, I16H)	L		0.90



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FIG. 46A

Variant	Sequence	Inhibition Ki (nM)			
		Kallikrein	Plasmin	XIIa	Xa
Aprotinin	RPDFCLEPPYTGPCAKARIIRYFYNAGAGLQQTFFYGGCRAKRNFKSAEDCHRTCGGA	20.00	0.23	5000.0	
Aprotinin R15, S42	DFCLEPPYTGPCARARIIRYFYNAGAGLQQTFFYGGCRAKSNFKSAEDCHRTCGGA	0.91	0.17	3983.0	
KPI (-4-57)	EVVREVCSEQAETGPCRAHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	45.00	34.00	3718.0	161.0
TW6167	EVVREVCSEQAETGPCRAHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	61.00		3641.0	288.0
BG031	EVVREVCSEQAETGPCRAHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	34.00		498.0	
BG032	EVVREVCSEQAETGPCRAHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	49.00		731.0	
TW101	EVCSEQAETGPCRAHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	2000.00	11.50		
TW6208	EVVREVCSEQAETGPCRGHISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI			369.0	
TW106	EVCSEQAETGPCRARISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	560.00	3.70		
DD108	EVVREVCSEQAETGPCRAAISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	1.70	11.20	1600.0	123.0
DD109	EVVREVCSEQAETGPCRAISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	9.50		1681.0	421.0
DD110	EVVREVCSEQAETGPCRALISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	2.10		624.0	55.0
DD111	EVVREVCSEQAETGPCRASISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	5.60			
DD112	EVVREVCSEQAETGPCRAVISRWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	6.80		998.0	
TW6179	EVVREVCSEQAETGPCRAGISRHWYFDVTEGKCAPFFYGGCGGNRNHFDTEEYCHAVCGSAI	78.00		368.0	



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FIG. 46B

TW6163	EVVREVCSEQAETGPCRAHHSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	4.70	103.58	4532.0	457.0
TW6172	EVVREVCSEQAETGPCRAKASRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	315.00			1463.0
TW6180	EVVREVCSEQAETGPCRAHPSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	70.00		885.0	39.0
TW6181	EVVREVCSEQAETGPCRAHKSRSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	150.00		1514.0	
BG001	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	38.00	10.00	489.0	204.0
TW116	EVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	145.00	89.00		806.0
DD102	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	16.00		315.0	
DD103	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	17.00		2128.0	110.0
DD104	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	15.00		237.0	345.0
DD105	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	18.00		198.0	320.0
TW6168	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	25.80		3521.0	395.0
TW6182	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	36.00		752.0	
TW6194	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	70.83			
TW6210	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	54.00		277.0	
CL006	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	110.20		89600.0	133.0
BG012	EVVREVCSEQAETGPCRAHLSRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI			40.0	116.0



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FIG. 46C

TW6209	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	81.00	45.90	184.0	613.0
TW6211	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	184.00		402.0	
DD128	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	44.00			37.0
TW6142	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	18.00	18.00	7972.0	225.0
AL301	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	216.00		1557.0	
AL302	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	39.00			316.0
TW6147	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	35.00		1090.0	179.0
TW6138	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	18.00		921.0	309.0
TW6154	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	11.00		915.0	39.0
TW6155	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	11.00			27.0
TW6140	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	35.00		475.0	
TW6156	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI				
TW6141	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	42.00			
TW118	EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	6.00	24.00	13009.0	68.0
DD100	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	15.00			
TW6157	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	40.00		511.0	168.0
TW6158	EWREVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTTEYCHAVCGSAI	29.00			





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FIG. 46D

TW6159	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	17.00			64.0
TW6161	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	7.50	18.00	1507.0	8.7
DD101	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	64.00		924.0	
TW6151	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	163.00		1162.0	954.0
TW6139	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	19.00	22.80	152.0	78.0
TW6153	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	11.20	21.30	65.0	36.0
TW122	EVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	32.00	27.00		581.0
TW6178	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	16.00		444.0	
TW6148	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	40.00			
TW124	EVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	64.00	48.00		
TW6149	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	54.00			
TW6173	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	1.00	7.24	1432.0	
TW6174	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	0.90	6.89	2796.0	
BC002	EVRVVCSEQAETGPRAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	0.98	19.00	403.0	60.0
DD129	EVRVVCSEQAETGPRALFISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	3.60		1864.0	6.0
DD185	EVRVVCSEQAETGPRCAAIFRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	0.39	8.71	150.0	196.0



10026604, 056324

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FIG. 46E

TW6165	EVVREVCSEQAETGPCRAAIIHRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	0.65	16.40	206.0
TW6166	EVVREVCSEQAETGPCRAAIYRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	0.4	10.10	73.0
BG028	EVVREVCSEQAETGPCRALIYRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	1.10	12.10	93.8
TW6169	EVVREVCSEQAETGPCRALILRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	1.20		619.0
DD113	EVVREVCSEQAETGPCRALIPRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	0.85	12.80	293.0
TW6175	EVVREVCSEQAETGPCRALIFRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	0.50	7.46	35.0
TW6201	EVVREVCSEQAETGPCRAGIYRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	34.60		419.0
TW6202	EVVREVCSEQAETGPCRAGIWRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	128.50		1237.0
TW6203	EVVREVCSEQAETGPCRAGIPRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	31.20		5045.0
TW6204	EVVREVCSEQAETGPCRAAISAWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI			147.0
TW6205	EVVREVCSEQAETGPCRALISAWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI			195.0
DD114	EVVREVCSEQAETGPCRAAISRWYFDVTEGKCAPFFYGGCGRGRNNFDTTEYCHAVCGSAI	0.70	7.77	224.0
TW6190	EVVREVCSEQAETGPCRAAISRWYFDVTEGKCAPFFYGGCYGRRNNFDTTEYCHAVCGSAI	0.83	52.20	589.0
TW6183	EVVREVCSEQAETGPCRAMHFRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	1.20	11.68	12440.0
TW6184	EVVREVCSEQAETGPCRAMHYRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	0.91	11.96	14000.0
TW6185	EVVREVCSEQAETGPCRAMHWRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	1.30	18.60	388.0
BG003	EVVREVCSEQAETGPCRAMLHRWYFDVTEGKCAPFFYGGCGGRRNNFDTTEYCHAVCGSAI	36.00		467.0



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FIG. 46F

TW6186	EVVREVCSEQAETGPCRAHHSRWYFDVTEGKCAPFFYGGCYGNRNNFDTEEYCHAVCGSAI	0.48	8.86	186.0	11.0
TW6187	EVVREVCSEQAETGPCRAHIFRWYFDVTEGKCAPFFYGGCYGNRNNFDTEEYCHAVCGSAI	3.80	15.40	92.0	15.0
TW6188	EVVREVCSEQAETGPCRAHIVRWYFDVTEGKCAPFFYGGCYGNRNNFDTEEYCHAVCGSAI	4.00		419.0	24.0
TW6189	EVVREVCSEQAETGPCRAHINRWYFDVTEGKCAPFFYGGCYGNRNNFDTEEYCHAVCGSAI	4.00			34.0
TW6170	EVVREVCSEQAETGPCRALILRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	2.50			452.0
DD115	EVVREVCSEQAETGPCRGYITRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI			213.0	299.0
DD170	EVVREVCSEQAETGPCRALHNRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	0.99	18.00	550.0	
TW6176	EVVREVCSEQAETGPCRAAHFRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	3.50	118.00	56.0	
TW6177	EVVREVCSEQAETGPCRALHFRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	7.20	32.70	245.0	156.0
BG006	EVVREVCSEQAETGPCRAALFRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	0.30	12.10	80.0	
DD130	EVVREVCSEQAETGPCRALTRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	5.50			9.5
DD131	EVVREVCSEQAETGPCRALFKRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	7.90	2.00	1385.0	3.3
DD132	EVVREVCSEQAETGPCRAFFKRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	112.00			16.8
DD120	EVVREVCSEQAETGPCRAAFSAWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	8.30			11.0
DD121	EVVREVCSEQAETGPCRALLSAWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	19.00			21.0
BG014	EVVREVCSEQAETGPCRALIHWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCHAVCGSAI	9.20	18.70	18.0	



# Title: PROTEASE INHIBITOR PEPTIDES

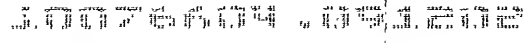
Inventor(s): R. Tyler WHITE et. al

Serial No. 10/076,604

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FIG. 46G

DD122	EVVREVCSEQAETGPCRALIFAHYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	15.00			46.0
BG015	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	6.00	12.20	19.4	597.0
BG020	EVVREVCSEQAETGPCRAAIHKWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	1.70		106.0	
BG022	EVVREVCSEQAETGPCRAAIYHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	0.64	7.26	14.5	
BG023	EVVREVCSEQAETGPCRALIQHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	23.00		262.0	
BG024	EVVREVCSEQAETGPCRALIYKWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	4.10	7.47	38.7	
BG027	EVVREVCSEQAETGPCRAAIQHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	5.80		144.0	
DD116	EVVREVCSEQAETGPCRAAIFRWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	0.14		583.0	84.0
TW6191	EVVREVCSEQAETGPCRAAIFRWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	0.26		664.0	20.0
DD117	EVVREVCSEQAETGPCRALIPRWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	0.11		1034.0	99.0
BG029	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	3.20		7.9	
BG030	EVVREVCSEQAETGPCRALIYHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	4.60		26.1	
BG033	EVVREVCSEQAETGPCRAAIYHWYFDVTEGKCAPPFYGGCGGNRRNFDTEEYCHAVCGSAI	0.75		5.6	



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BG034	EVVREVCSEQAESGPCRAAIYHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	0.47	18.5
BG040	EVVREVCSEQAEGPCRALIYHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	3.40	8.6
BG016	EVVREVCSEQAETGPCRGAIQHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	160.00	178.0
BG017	EVVREVCSEQAETGPCRGAIRHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	180.00	200.0
BG021	EVVREVCSEQAETGPCRGSIRHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	340.00	224.0
BG025	EVVREVCSEQAETGPCRGLIYHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	65.00	16.2
BG026	EVVREVCSEQAETGPCRGAIIYHWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	50.00	34.9
DD118	EVVREVCSEQAETGPCRALHNRWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	0.53	
DD134	EVVREVCSEQAETGPCRALFKRWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	1.10	15640.0
DD135	EVVREVCSEQAETGPCRALFKRWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	1.30	7473.0
DD136	EVVREVCSEQAETGPCRALFKRWYFDVTEGKCAPPFYGGCGNRNPNFTTEYCHAVCGSAI	1.10	1.8



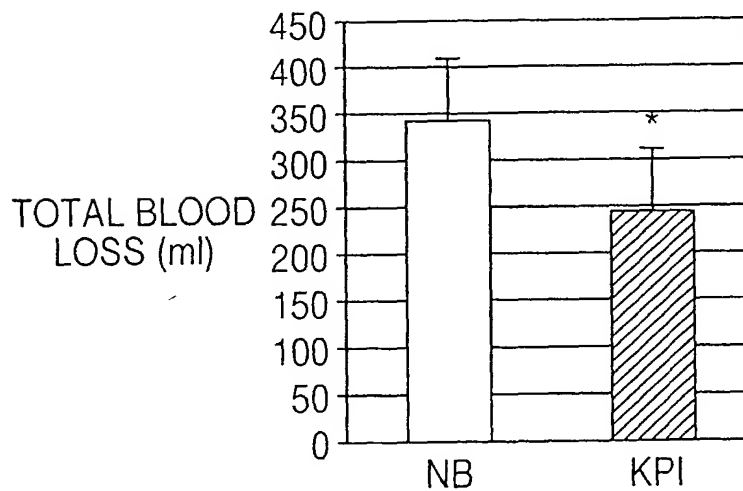
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## FIG. 47

### VOLUMES

NS	344.25
KPI	245.75

	KPI	NS
	298	366
	266	342
	354	294
	258	385
	168	288
	266	469
	172	338
	184	272
MEAN	245.75	344.25
STDEV	66.2414415	63.97488346
TTEST	0.009094999	





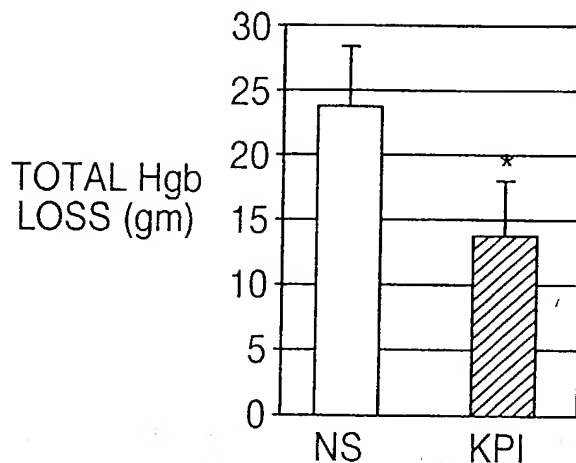
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## FIG. 48

### HEMOGLOBIN

NS	23.61
KPI	13.59

	KPI	NS
	16.58	24.95
	15.19	24.87
	20.21	20.46
	8.99	27.59
	14.63	18.23
	15.31	31.59
	7.7	23.26
	10.14	17.96
MEAN	13.59375	23.61375
STDEV	4.261438	4.68761
TTEST		0.000536





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FIG. 49

PaO2

	Baseline PaO2		End CPB		Obs 60 min		Obs 180 min	
	KPI	NS	KPI	NS	KPI	NS	KPI	NS
MEAN	652.2	670.9	495.7	60.5	483.7	441.3	391.3	
STDEV	654	559.2	444.6	132.2	330.1	448.7	264.1	484.6
TTEST	596.2	622.9	170.2	93.8	415.4	85.1	416.5	81.3
	606.2	689.2	264.2	333.9	430.2	529.6	361.9	333.2
	633.1	665.1	567.2	341.7	613	568.3	90.8	546.6
	646.6	527	507.4	226.9	564.3	438.1	518.2	485.3
	563.2	461.7	547.1	89.1	501	42.6	494.2	45.6
	659.9	508	416.6	59.7	504.5	405.8	452	383.7
	626.425	588	426.625	167.225	480.275	369.938	371.1	344
	34.4692	85.5055	140.474	117.993	88.6187	196.523	150.277	186.22
	3	6	1	1	9	5	4	7
	p=	0.268	p=	0.0014	p=	0.17915	p=	0.76

N.S.

N.S.



# FIG. 50

## Summary of Data

### Total Volumes

	Total volume loss	Total Hgb Loss
KPI-1	298	16.58
KPI-2	266	15.19
KPI-3	354	20.21
KPI-4	258	8.99
KPI-5	168	14.63
KPI-6	266	15.31
KPI-7	172	7.7
KPI-8	184	10.14

MEAN	245.75	13.59
STDEV	66.24	4.26

NS-1A	366	24.95
NS-2	342	24.87
NS-3	294	20.46
NS-4	385	27.59
NS-5	288	18.23
NS-6	469	31.59
NS-7	338	23.26
NS-8	272	17.96

MEAN	344.25	23.61
STDEV	63.97	4.69

\*p = 0.009

\*p = 0.0005

### Serial Chest tube Hbg

	0-30min	30-60min	60-120min	120-180min
	3.7	4.3	8.6	6.2
	4.3	6.4	6.7	5.7
	4.1	4.4	7	7.1
	2.8	4	4.4	1.9
	6.3	6.5	7	6.7
	4.1	6.1	5.6	6.3
	3.1	4.6	5.4	4.4
	6.9	5.8	5.4	4.2

MEAN	4.41	5.26	6.26	5.3
STDEV	1.45	1.04	1.32	1.72

	7.7	8.6	6.1	5.4
	7.2	7.4	7.6	7.1
	5.4	7.5	7.5	6.5
	8.4	7.2	7.1	6.3
	7.5	7.2	5.2	5.6
	4	7	7.3	7.4
	7.5	7.7	5.8	4.2
	7.4	8.2	6	5.3

MEAN	6.89	7.6	6.58	6.1
STDEV	1.44	1.04	0.91	0.85

\*p = 0.004 \*p = 0002

NS

NS



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